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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,451	MILLER ET AL.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-16-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment and IDS dated 8-16-04 is acknowledged.

Claims 1-8 and 11-25 are pending.

The following outstanding rejection from previous office action dated 4-14-04 is maintained:

1. Claims 1-4, 6-8, 11-16 and 18-25 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 89/09066 (hereafter WO '066).

WO '066 discloses a controlled release composition comprising an active agent, a polymeric matrix comprising a water-soluble polymer and a surface-active agent, for a zero order relelase rate (abstract, page 13, last paragraph; page 14, lines 14-18). The surface-active agents of WO '066 include fatty acid esters and fatty acid ethers having 12 to 24 carbon atoms, which read on the instant hydrophobic fusible agents (page 7, lines 23 to page 8, line 4). WO does not state the melting point, however, instant specification also include fatty acid esters and fatty acid ethers as suitable fusible materials and accordingly, WO '066 meet the claimed requirement. WO '066 discloses polyethylene glycol as a suitable hydrophilic material and recites the molecular weight of PEG that is within the ranged disclosed in the instant specification (page 9, lines 4-17). WO '066 further discloses that the active agent will have a particle size in the range of 0.1 to 500 microns and also disclose multiparticulate forms (page 11; page 17, lines 27-35). With respect to the claimed "extrudate", WO discloses that the composition is extruded (page 18, lines 18-30; page 19, lines 1-5 & lines 12-16 & page 20, lines 8-14). With respect to the claimed water soluble substance, in particular, morphine and the release rates, WO '066 discloses morphine hydrochloride preparation in example of (page 28), where the composition comprises a matrix

formed of a molten mixture of hydrophilic polymer (dextrin) and PEG monostearate was extruded. Thus, WO '066 meets the limitations of claims 6, 13, 19 and 21.

With respect to the claimed release rates (of claims 1-3 and14-17), dissolution parameters i.e., ratio of Cmax to mean plasma levels, tmax, W50 etc., and the claimed test method, it is examiner's position that because WO '066 discloses claimed polymers of the matrix and also morphine, the release rates claimed are inherent to the compositions. WO '066 further discloses that the release of the active agent is achieved for a long time i.e., 8 hours or more (table on page 32). With respect to claim 11, the limitation "the dosage form being obtainable by a process comprising:" even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." With respect to claims 8, 22 and 23, "suitable for once-a-day dosing" is an intended limitation that carries no patentable weight. Therefore, for the reasons above, WO '066 anticipates instant claims.

2. Claims 1-4, 8, 11, 12, 14-16 and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,828,836 to Elger et al (hereafter Elger).

Elger discloses a solid, controlled release pharmaceutical formulation comprising an active agent incorporated in a controlled release matrix comprising a water-soluble polydextrose, for achieving a slow relelase of drug over extended periods of time. (Col. 1). Elger discloses that the matrix also contains at least one digestible C8-C50 substituted or unsubstituted hydrocarbon,

especially a C12-C36 fatty alcohol such as polyethylene glycol and optionally contains hydroxyalkyl or carboxyalkylcellulose (col. 2, lines 11-35). The matrix polymer, polydextrose, and polyethylene glycol taught by Elger read on the instant matrix materials. Although Elger does not state the melting point as claimed, the property is inherent to the compounds because instant specification also states polyethylene glycol as the suitable hydrophobic agent having the claimed melting point. Elger also discloses tablets and capsule, as claimed. The teachings of pellets and granules by Elger meet the claimed particulates because the instant claims do not state the particle size. With respect to the limitations regarding specific release rates, dissolution parameters i.e., ratio of Cmax to mean plasma levels, tmax, W50 etc., and the claimed test method, it is examiner's position that because Elger discloses claimed polymers of the matrix and also discloses various active agents (col. 3) that include the water soluble active agents (for and also discloses various active agents (col. 3) that include the water soluble active agents (for example theophylline in col. 8 and pyridoxine hydrochloride in col. 8, both of which are water soluble), the release rates claimed are inherent to the compositions. Elger further discloses that the release of the active agent is achieved for a long time i.e., 8 hours or more (col. 1, lines 7-12) and figure 2 shows that the release is achieved over 15 –20 hours.

Claim Rejections - 35 USC § 103

3. Claims 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 89/09066 (WO '066).

WO '066 discussed above fails to teach the instant ratios of hydrophobic and hydrophilic components of matrix. However, WO '066 teaches the compositions for controlled zero order relelase rates of active agents (page 11) and also teaches the claimed morphine compounds. Further, WO '066 teaches that the combination of surface-active agents and the polymer in the matrix enable the release of drug at a substantially constant rate. Therefore, it would have been within the scope of a skilled artisan at the time of the instant invention to optimize the amounts of surface-active agents and the soluble polymer in the formulation of WO '006 such that a homogenous matrix is obtained which provides a zero order release rate of the active agent.

4. Claims 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elger et al (hereafter Elger).

Instant claims recite a specific ratio of hydrophobic fusible agent and the polymer.

Elger, discussed above, fails to teach exactly the same ratios as claimed, 8:1 to 16:1 and instead teaches a ratio of 1:4 to 4:1. However, the examples of solid controlled relelase compositions taught by Elger (in cols. 7 and 8), Elger teaches a higher amount of hydrophobic polyethylene glycol as compared to polydextrose. Further, Elger teaches the above matrix components for the same purpose as claimed. Accordingly, optimizing the amounts of the hydrophobic and hydrophilic agents in the compositions of Elger so as to achieve a sustained

release rate of a given active agent would have been obvious for one of an ordinary skill in the art.

5. Claims 1-8 and 11-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,965,163. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant solid, oral, controlled relelase formulations are generic to the particulate solid dosage forms of the patented claims because instant dependent claim recite microparticulates. Besides, both sets of claims recite the similar of matrix and also morphine as the active agent in the dependent claims. Instant claim 11 recites the product by process claim, which overlaps with the patented product by process claims. Absent any distinction in the active agent or matrix materials, the patented solid dosage form inherently possess the ability to produce the claimed release rates, as tested by the specified method of instant claims. Accordingly, the species of the patented claims anticipates the claimed genus of the instant application, and therefore, a patent to the genus would necessarily, extend the rights of the species should the genus issue as a patent after the species.

Response to Arguments

Applicant's arguments filed 8-16-04 have been fully considered but they are not persuasive.

Rejection over WO 89/09066 (WO): Applicants argue that WO neither teaches nor suggests a formulation, which provides the combined features of releasing 15% to 45% of the drug load

over 8 hours at a zero order rate and has a Cmax/C24 ratio of 1.5 to 3.5. In support of the argument, applicants cite several of the examples of WO and state that it would be impossible with the composition from those examples to achieve the release rates claimed in the instant application. Applicants argue that examiner's assumption and analysis that because certain of the excipients and active ingredients of WO are same as the instant the claimed release rates are inherent to the compositions of WO is unscientific and erroneous. Applicants' arguments have been considered but not found persuasive because WO clearly discloses a zero order release composition containing matrix made of a soluble polymer and a hydrophobic surfactant and an active agent. Applicants have not presented any argument regarding the teachings of the claimed components by WO. With respect to applicants' interpretation of the reference (WO) examples, the explained release rates are merely speculative and speculation without experimental evidence is not persuasive. Besides, while instant claims recite a specific release rate with the claimed method of measurements, it is unclear as to what method of measurement are the speculated release rates of WO are based upon. Further, while instant claim 1 do not specify any specific drug or a polymeric matrix that would exhibit the claimed relelase rates, Further, WO discloses a composition comprising morphine hydrochloride as an active agent, which is also claimed by the instant invention. Further, example 10 e and 10 f of WO are directed to morphine compostions, one of the drugs claimed in the instant application. If applicants' arguments are true that the above examples of WO do not result in the claimed release rate, applicants have not explained what method has been employed to measure the argued release rates, is the difference due to a method of measurement or due to the specific matrix or a specific drug or what drug in the instant application results in the release rate. Accordingly, in the absence of a proper comparison,

the mere speculative arguments are not persuasive, as the specific release rate is dependent upon the active, amount of the active and the specific matrix materials employed (see page 3, lines 23-34).

With respect to claims 5 and 17, applicants argue that the reference teaches away from the claimed high amounts of surface-active agent because WO states that above 50% by weight of surface-active agent, there is a phase inversion and may become a continuous phase. However, as explained in above paragraph, WO also states that the specific release of an active agent depends upon the active as well as the matrix components. Further, WO also states that the active agent itself can have the surfactant properties. Furthermore, instant claimed release rates are not presented as a positive limitation and instead as an intended use. Therefore, applicants' argument that the proposed modification changes the principle of operation is moot.

Double patenting rejection: In response to the terminal disclaimer filed the double patenting rejection over US 6,399,096 has been withdrawn. However, applicants' arguments regarding the double patenting rejection over US 5,965,163 are not persuasive because applicants' merely stated that the very least, the zero order release of the present claims is not obvious and did not explain the reasons for nonobviousness.

Rejection over Elger et al (US 4,828,836):

Applicants argue that Elger fails to teach any product, which has a zero order release rate over the first eight hours and the in-vitro data of Elger shows that the active agent in released in a first order profile. Applicants' arguments are not persuasive because as explained in the

rejection, Elgers teaches all the structural limitation of the instant composition that has been claimed. Applicants have not argued regarding the teachings of the claimed soluble material, and the hydrophobic and hydrophilic materials comprising the matrix (of Elger). The claimed release profile is an intended use and does not constitute a positive limitation. With respect to the argument that Elgers only teaches theophylline, instant claims are broader in scope with respect to any soluble active agent and accordingly includes the drug taught by Elgers. With respect to the examiner's position regarding the inherency of the release rates to the composition, Applicants' argue that release rates are affected by many factors, including the proportion of the ingredients, the manner they are put together, processing conditions and so forth. However, applicants also emphasize that the "missing descriptive material" should be necessarily present in order to maintain inherent anticipation and states that the claimed parameters are not necessarily present. Applicants' arguments are not persuasive because while admitting that release rates are dependent upon a number of factors, applicants have not shown that it is possible for the instant claimed water-soluble agent (includes any or all of the known soluble active agent) and a matrix produce the same release parameters claimed. Further, if it is assumed that the release rates are independent of the factors above, then the composition of Elger comprising a soluble active agent and the claimed matrix components should necessarily possess the "descriptive material" argued. Instant claims do not recite any more descriptive material than a soluble active agent and a matrix, which are taught by Elger and the claimed release rates do not constitute a positive limitation. Accordingly, the rejection over the teachings of Elger has been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615
December 16, 2004

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